General

Guideline Title

EGFR-TK mutation testing in adults with locally advanced or metastatic non-small-cell lung cancer.

Bibliographic Source(s)

National Institute for Health and Care Excellence (NICE). EGFR-TK mutation testing in adults with locally advanced or metastatic non-small-cell lung cancer. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Aug. 46 p. (Diagnostics guidance; no. 9).

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

The tests and test strategies listed below are recommended as options for detecting epidermal growth factor receptor tyrosine kinase (EGFR-TK) mutations in the tumours of adults with previously untreated, locally advanced or metastatic non-small-cell lung cancer (NSCLC), when used in accredited laboratories participating in an external quality assurance scheme. The laboratory-developed tests should be designed to detect the mutations that can be detected by one of the CE-marked tests as a minimum.

- therascreen EGFR RGQ PCR Kit (CE-marked)
- cobas EGFR Mutation Test (CE-marked)
- Sanger sequencing of samples with more than 30% tumour cells and therascreen EGFR RGQ PCR Kit for samples with lower tumour cell contents
- Sanger sequencing of samples with more than 30% tumour cells and cobas EGFR Mutation Test for samples with lower tumour cell contents
- Sanger sequencing followed by fragment length analysis and polymerase chain reaction (PCR) of negative samples.

There was insufficient evidence for the Committee to make recommendations on the following methods:

- High-resolution melt analysis
- Pyrosequencing combined with fragment length analysis
- Single-strand conformation polymorphism analysis
- Next-generation sequencing
- therascreen EGFR Pyro Kit (CE-marked)

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Locally advanced or metastatic non-small-cell lung cancer (NSCLC)

Guideline Category

Diagnosis

Evaluation

Management

Technology Assessment

Clinical Specialty

Internal Medicine

Medical Genetics

Oncology

Pathology

Pulmonary Medicine

Intended Users

Advanced Practice Nurses

Clinical Laboratory Personnel

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To identify which tests and test strategies for epidermal growth factor receptor tyrosine kinase (EGFR-TK) mutation testing in adults with previously untreated, locally advanced or metastatic non-small-cell lung cancer (NSCLC) are clinically and cost-effective for informing first-line treatment decisions as currently recommended by National Institute of Health and Care Excellence (NICE)

Target Population

Adult patients with untreated locally advanced or metastatic non-small-cell lung cancer (NSCLC) who may benefit from first-line treatment with epidermal growth factor receptor tyrosine kinase (EGFR-TK) inhibitors

Interventions and Practices Considered

Epidermal growth factor receptor tyrosine kinase (EGFR-TK) mutation testing:

- therascreen EGFR RGQ PCR Kit (CE-marked)
- cobas EGFR Mutation Test (CE-marked)
- Sanger sequencing of samples with more than 30% tumour cells and therascreen EGFR RGQ PCR Kit for samples with lower tumour cell contents
- Sanger sequencing of samples with more than 30% tumour cells and cobas EGFR Mutation Test for samples with lower tumour cell contents
- Sanger sequencing followed by fragment length analysis and polymerase chain reaction (PCR) of negative samples

Note: There was insufficient evidence for the Committee to make recommendations on the following testing methods: high-resolution melt analysis, pyrosequencing combined with fragment length analysis, single-strand conformation polymorphism analysis, next-generation sequencing, therascreen EGFR Pyro Kit (CE-marked).

Major Outcomes Considered

- Technical performance characteristics of different epidermal growth factor receptor (EGFR) tests
- EGFR mutation test accuracy
- Test failure rates
- Response to treatment (objective response, progression-free survival, overall survival, disease control)
- Cost-effectiveness

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Care Excellence (NICE) commissioned an External Assessment Group to perform a systematic literature review on the technology considered in this diagnostics guidance and prepare a Diagnostics Assessment Report (DAR). The DAR for this guidance was prepared by Kleijnen Systematic Reviews Ltd in collaboration with Erasmus University Rotterdam and Maastricht University (see the "Availability of Companion Documents" field).

Assessment of Clinical Effectiveness

Systematic Review Methods

Search Strategy

Search strategies were based on target condition and intervention, as recommended in the Centre for Reviews and Dissemination (CRD) guidance for undertaking reviews in health care and the Cochrane Handbook for Diagnostic Test Accuracy Reviews.

Candidate search terms were identified from target references, browsing database thesauri (e.g., Medline MeSH and EMBASE Emtree), existing reviews identified during the rapid appraisal process and initial scoping searches. These scoping searches were used to generate test sets of target references, which informed text mining analysis of high-frequency subject indexing terms using Endnote reference management software. Strategy development involved an iterative approach testing candidate text and indexing terms across a sample of bibliographic databases and aimed to reach a satisfactory balance of sensitivity and specificity.

The following databases were searched for relevant studies from 2000 to August 2011:

- MEDLINE (OvidSP) (2000-2012/07/wk 1)
- MEDLINE In-Process Citations and Daily Update (OvidSP) (up to 2012/07/17)
- EMBASE (OvidSP) (2000-2012/wk 28)
- Cochrane Database of Systematic Reviews (CDSR) (Internet) (2000-2012/Issue 7)
- Cochrane Central Register of Controlled Trials (CENTRAL) (Internet) (2000-2012/Issue 7)
- Database of Abstracts of Reviews of Effects (DARE) (via Cochrane Library) (2000-2012/Issue 3)
- Health Technology Assessment Database (HTA) (via Cochrane Library) (2000-2012/Issue 3)
- Science Citation Index (SCI) (Web of Science) (2000-2012/07/18) LILACS (Latin American and Caribbean Health Sciences Literature) (Internet) (2000-2012/07/06) http://regional.bvsalud.org/php/index.php?lang=en
- Biosis Previews (Web of Knowledge) (2000-2012/08/24)
- NIHR Health Technology Assessment Programme (Internet) (2000-2012/07/18)
- PROSPERO (International Prospective Register of Systematic Reviews) (Internet) (up to 2012/07/19) http://www.crd.york.ac.uk/prospero/

Completed and ongoing trials were identified by searches of the following resources:

- NIH ClinicalTrials.gov (2000-2012/07/19) (Internet) http://www.clinicaltrials.gov/
- Current Controlled Trials (2000-2012/08/30) (Internet)
- WHO International Clinical Trials Registry Platform (ICTRP) (2000-2012/08/30) (Internet) http://www.who.int/ictrp/en

Searches were undertaken to identify studies of epidermal growth factor receptor tyrosine kinase (EGFR-TK) mutation testing in non-small-cell lung cancer (NSCLC). The main EMBASE strategy for each set of searches was independently peer reviewed by a second Information Specialist, using the PRESS-EBC checklist. Search strategies were developed specifically for each database and the keywords associated with NSCLC were adapted according to the configuration of each database. Searches took into account generic and other product names for the intervention. No restrictions on language or publication status were applied. Limits were applied to remove animal studies. Full search strategies are reported in Appendix 1 in the DAR.

Electronic searches were undertaken for the conference abstracts. Refer to the Assessment Report for web sites and dates searched.

Identified references were downloaded in Endnote X4 software for further assessment and handling. References in retrieved articles were checked for additional studies. The final list of included papers was also checked on PubMed for retractions, errata, and related citations.

Inclusion and Exclusion Criteria

Separate inclusion criteria were developed for each of the three clinical effectiveness questions; these are summarised in Table 2 in the DAR.

Inclusion Screening

Two reviewers independently screened the titles and abstracts of all reports identified by searches and any discrepancies were discussed and resolved by consensus. Full copies of all studies deemed potentially relevant were obtained and the same two reviewers independently assessed these for inclusion; any disagreements were resolved by consensus. Details of studies excluded at the full paper screening stage are presented in Appendix 5 in the DAR.

Studies provided by the manufacturers of therascreen®, and cobas® EGFR Mutation Testing Kit were first checked against the project reference database, in Endnote X4; any studies not already identified by the searches were screened for inclusion.

Assessment of Cost-effectiveness

Review of Economic Analyses of EGFR Mutation Testing

Search Strategy

Searches were undertaken to identify cost-effectiveness studies of EGFR-TK testing in NSCLC. As with the clinical effectiveness searching, the main EMBASE strategy for each set of searches was independently peer reviewed by a second Information Specialist, using the PRESS-EBC checklist. Search strategies were developed specifically for each database and searches took into account generic and other product names for the intervention. All search strategies are reported in Appendix 1 in the DAR.

The following databases were searched for relevant studies from 2000 to present:

- MEDLINE (OvidSP) (2000-2012/09/wk4)
- MEDLINE In-Process Citations and Daily Update (OvidSP) (2000-2012/08/29)
- EMBASE (OvidSP) (2000-2012/wk 34) National Health Service Economic Evaluation Database (NHS EED) (via Cochrane Library) (2000-2012/Issue 3)
- Health Economic Evaluation Database (HEED) (Wiley) (2000-2012/08/30) http://onlinelibrary.wiley.com/book/10.1002/9780470510933
- Science Citation Index (SCI) (Web of Science) (2000-2012/08/29)

Additional searches were undertaken to update the Resource Utilisation searches in the Manufacturer's submission for Single Technology Appraisal (STA) 192. (Refer to Section 4.1.1 in the DAR for the list of resources searched.)

Identified references were downloaded in Endnote X4 software for further assessment and handling. References in retrieved articles were checked for additional studies.

Inclusion Criteria

Studies reporting a full economic analysis, which related explicitly to the test-treat combination of EGFR mutation testing and treatment with EGFR tyrosine kinase inhibitors (TKIs), were eligible for inclusion. Specifically, one of the comparators included EGFR mutation testing and for this comparator the treatment decision was guided by the test result; patients whose tumour was EGFR-mutation negative were also included in the treatment pathway.

Studies were independently assessed for inclusion by two health economists, and any disagreements were resolved by discussion.

Number of Source Documents

Assessment of Clinical Effectiveness

The literature searches of bibliographic databases identified 6,932 references. After initial screening of titles and abstracts, 152 were considered to be potentially relevant and ordered for full paper screening. One conference abstract, which was provided as part of the submission from one of the manufacturers, was included in the review. No additional studies were identified from searches of clinical trials registries.

Based on the searches and inclusion screening, 31 publications of 11 studies were included in the review. Hand searching of conference proceedings resulted in the identification of two additional publications for two previously identified trials. A total of 11 studies in 33 publications were therefore included in the review.

Figure 1 in the Diagnostics Assessment Report (DAR) (see the "Availability of Companion Documents'" field) shows the flow of studies through the review process. See Appendix 5 in the DAR for reasons for exclusions of all publications excluded at the full paper screening stage.

Assessment of Cost-effectiveness

- The search retrieved 606 references. After initial screening of titles and abstracts, four studies remained, all of which were published as conference abstracts only. Two additional studies were identified, one published as a conference abstract only and one published as a full paper and a conference abstract; the latter did not fully meet the inclusion criteria, as it concerned second-line treatment of advanced non-small-cell lung cancer (NSCLC) with erlotinib. In total, six studies were included, of which only one was published as a full paper.
- An economic model was submitted.

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus (Committee)

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Care Excellence (NICE) commissioned an Expert Assessment Group to perform a systematic literature review on the technology considered in this appraisal and prepare a Diagnostics Assessment Report (DAR). The DAR for this guidance was prepared by Kleijnen Systematic Reviews Ltd in collaboration with Erasmus University Rotterdam and Maastricht University (see the "Availability of Companion Documents" field).

Assessment of Clinical Effectiveness

Systematic Review Methods

Data Extraction

Data were extracted on the following: study design/details, participant details (e.g., tumour stage, histological diagnosis, performance status, smoking status, ethnicity), epidermal growth factor receptor (EGFR) mutation test(s) and mutations targeted, clinical outcomes, test performance outcome measures (against treatment response as reference standard), details of specific mutations identified by outcome measure (where reported) and test failure rates. Data were extracted by one reviewer, using a piloted, standard data extraction form and checked by a second; any disagreements were resolved by consensus. Full data extraction tables are provided in Appendix 2 in the DAR.

Quality Assessment

The risk of bias in included randomised controlled trials (RCTs) was assessed using the Cochrane Collaboration's tool for assessing risk of bias in randomised trials. Studies used to derive accuracy data, for the ability of EGFR mutation tests to predict treatment response, were assessed using QUADAS-2. Studies which provided both accuracy data and data on the effectiveness of treatment with tyrosine kinase inhibitors (TKIs) following testing were assessed using both tools. Risk of bias assessments was undertaken by one reviewer and checked by a second reviewer, and any disagreements were resolved by consensus.

The results of the risk of bias assessments were summarised and presented in tables and graphs in the results of the systematic review and are presented in full, by study, in Appendix 3 in the DAR.

Survey of Laboratories Providing EGFR Mutation Testing

The Assessment Group conducted a web-based survey to gather data on the technical performance characteristics of EGFR mutation tests. An e-mail invitation was sent to National Health Service (NHS) laboratories participating in the UK National External Quality Assurance Scheme (NEQAS) pilot scheme for EGFR mutation testing, who had responded to a request to provide information to NICE at the start of this assessment. Survey Monkey online software was used to run the survey. The survey was structured into sections on:

- Laboratory details
- EGFR testing methods
- Logistics Technical Methods
- Costs

Where possible the Assessment Group used multiple choice options with tick boxes to make the survey quick and easy to complete. A copy of the survey is provided in Appendix 4 in the DAR.

Methods of Analysis/Synthesis

The results of studies included in this review were summarised by research question (see Section 1 in the DAR), i.e., studies providing technical information on EGFR mutation testing in NHS laboratories in England and Wales, studies providing information on the accuracy of EGFR mutation tests for predicting response to TKI treatment, and studies reporting information on how clinical outcomes may vary according to which test is used to select patients for TKI treatment. The Assessment Group planned to use a bivariate/hierarchical summary receiver operating characteristic (HSROC) random effects model to generate summary estimates and a summary receiver operating characteristic (SROC) curve for test accuracy data, and a DerSimonian and Laird random effects model to generate summary estimates of treatment effects. However, because the review identified a relatively small number of studies with between study variation in participant characteristics, methods used to test for EGFR mutations and mutations targeted, the Assessment Group did not consider meta-analyses to be appropriate and has provided a structured narrative synthesis.

For all studies that provided data on accuracy for the prediction of response to treatment with TKIs, the absolute numbers of true positive, false negative, false positive and true negative test results, as well as sensitivity and specificity values, with 95% confidence intervals (CIs) are presented in results tables, for each reference standard response (e.g., objective response [OR], disease control [DC]) reported. Where reported, data on the numbers of failed EGFR mutation tests and reasons for failure were also included in the results tables. The results of individual studies were plotted in the receiver operating characteristic (ROC) plane to illustrate the trade-off between sensitivity and specificity and for ease of comparison between test methods; separate plots were provided for each reference standard response. For RCTs providing information on how clinical outcomes may vary according to which test is used to select patients for TKI treatment, hazard ratios (HRs), with 95% CIs, are provided survival outcome measures (progression-free survival [PFS] and overall survival [OS]) and relative risk (RR), with 95% CIs, are reported for tumour response outcomes (OR and DC). The results of individual studies were illustrated in forest plots. Between-study clinical heterogeneity was assessed qualitatively. There were insufficient studies to assess heterogeneity statistically such as the chi-squared test and I^2 statistic.

Assessment of Cost-effectiveness

Model Structure

The health economic analysis considers the long-term consequences of technical performance and accuracy of the different tests/test combinations followed by treatment with either standard chemotherapy or a TKI in patients with non-small-cell lung cancer (NSCLC). For this purpose a decision tree and a Markov model were developed. The decision tree was used to model the test result (positive, negative or unknown) and the treatment decision. Patients with a positive test result receive an anti-EGFR TKI. It is assumed that patients with a negative test result or unknown EGFR mutation status will receive doublet chemotherapy (Pemetrexed and Cisplatin), as the negative consequences of treatment with TKIs in false positives are greater than the negative consequences of treatment with doublet chemotherapy in false negatives. The decision tree is shown in Figure 10 in the DAR.

The long-term consequences in terms of costs and quality-adjusted life years (QALYs) were estimated using a Markov model with a cycle time of 21 days (resembling the duration of one cycle of chemotherapy), and a time horizon of six years. Health states in the Markov model are: progression free (subdivided into 'response' and 'stable disease'), disease progression and death. In the progression-free state, patients are on treatment (either TKI or doublet chemotherapy). In each cycle these patients are subdivided over the 'stable disease' and 'response' states, based on the objective response rate, in order to account for a difference in quality of life between those states. In addition, disutilities and costs associated with treatment related characteristics (intra-venous or oral therapy) are modelled. For adverse events of treatment, disutilities and costs were applied for a single cycle in the model. The Markov model structure is shown in Figure 11 in the DAR. The model is described in more detail in NICE Technology Appraisal 192 .

Refer to Section 4 in the DAR for additional information on cost-effectiveness analysis.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Developing Recommendations

After reviewing the evidence the Diagnostic Advisory Committee (DAC) agrees draft recommendations on the use of the technology in the National Health Service (NHS) in England. When formulating these recommendations, the Committee has discretion to consider those factors it believes are most appropriate to the evaluation. In doing so, the Committee has regard to any relevant provisions of the National Institute for Health and Care Excellence's (NICE's) Directions, set out by the Secretary of State for Health, and legislation on human rights, discrimination and equality. In undertaking evaluations of healthcare technologies, NICE takes into account the broad balance of clinical benefits and costs, the degree of clinical need of patients under consideration, any guidance issued to the NHS by the Secretary of State that is specifically drawn to the attention of NICE by the Secretary of State, and any guidance issued by the Secretary of State, and the potential for long-term benefits to the NHS of innovation.

The Committee takes into account advice from NICE on the approach it should take to making scientific and social value judgements. Advice on social value judgements is informed in part by the work of NICE's Citizens Council.

The Committee takes into account how its judgements have a bearing on distributive justice or legal requirements in relation to human rights, discrimination and equality. Such characteristics include, but are not confined to: race, gender, disability, religion or belief, sexual orientation,

gender reassignment and pregnancy or maternity.

The Committee considers the application of other Board-approved NICE methods policies, such as the supplementary guidance on discounting and the end-of-life criteria, if they are relevant to the evaluation.

Because the Programme often evaluates new technologies that have a thin evidence base, in formulating its recommendations the Committee balances the quality and quantity of evidence with the expected value of the technology to the NHS and the public.

The credibility of the guidance produced by NICE depends on the transparency of the DAC's decision-making process. It is crucial that the DAC's decisions are explained clearly, and that the contributions of registered stakeholders and the views of members of the public are considered. The reasoning behind the Committee's recommendations is explained, with reference to the factors that have been taken into account.

The language and style used in the documents produced by the Committee are governed by the following principles:

- Clarity is essential in explaining how the DAC has come to its conclusions.
- The text of the documents does not need to reiterate all the factual information that can be found in the information published alongside the guidance. This needs careful judgement so that enough information and justification is given in the recommendations to enable the reader to understand what evidence the DAC considered and, if appropriate, who provided that evidence.

The Committee may take into account factors that may provide benefits to the NHS or the population, such as patient convenience. It may also consider costs and other positive or negative impacts on the NHS that may not be captured in the reference-case cost analysis, such as improved processes.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

Results from the 'comparative effectiveness' analysis showed the therascreen epidermal growth factor receptor polymerase chain reaction (EGFR PCR) Kit to be both less effective and less costly compared with Sanger sequencing of exons 19 to 21, with an incremental cost-effectiveness ratio (ICER) of £32,167 saved per quality-adjusted life year (QALY) lost. Adjustments to costs and the proportions of patients with unknown mutation status in sensitivity analyses had little effect on the results. When treatment costs and adverse event costs were updated to 2012 costs, the ICER was £32,196 saved per QALY lost for the therascreen EGFR PCR Kit compared with Sanger sequencing. When the proportions of patients with unknown mutation status were based on the results from the web-based survey rather than information from published trials, the ICER was £34,555 saved per QALY lost for the therascreen EGFR PCR Kit compared with Sanger sequencing.

Results from the 'linked evidence' analysis also showed the therascreen EGFR PCR Kit to be both less effective and less costly than Sanger sequencing of exons 18 to 21 at an ICER of £31,849 saved per QALY lost. Sensitivity analyses had little effect on the results. When the treatment costs and adverse event costs were updated to 2012 costs, the ICER was £34,169 saved per QALY lost for the therascreen EGFR PCR Kit compared with Sanger sequencing of exons 18 to 21. When the proportions of patients with unknown mutation status were based on the results from the web-based survey rather than information from published trials, the ICER was £31,880 saved per QALY lost for the therascreen EGFR PCR Kit compared with Sanger sequencing of exons 18 to 21.

In the 'assumption of equal prognostic value' analysis, the comparative effectiveness, test accuracy and proportion of patients with unknown mutation status for each test strategy were assumed equal to those of the therascreen EGFR PCR Kit. Therefore, the test strategies only differed with respect to costs. Results showed that the test strategy of Sanger sequencing or the cobas EGFR Mutation Test for samples with insufficient tumour cells was the least expensive (£15 [0.06%] cheaper than Sanger sequencing of exons 18 to 21 alone), and fragment length analysis combined with pyrosequencing was the most expensive strategy (£33 [0.13%] more expensive than Sanger sequencing of exons 18 to 21 alone).

The External Assessment Group did not include next-generation sequencing and the therascreen EGFR Pyro Kit in any of the cost-effectiveness analyses because of a lack of data.

Considerations

The Diagnostics Advisory Committee noted that the analysis in National Institute for Health and Care Excellence (NICE) technology appraisal guidance 192 (Gefitinib for the first-line treatment of locally advanced or metastatic non-small-cell lung cancer) was primarily based on data from

the IPASS trial, which used the therascreen EGFR PCR Kit to classify tumours of patients as EGFR-tyrosine kinase (TK) mutation positive or negative. The Committee acknowledged that the recommendation of gefitinib for the first-line treatment of locally advanced or metastatic non-small-cell lung cancer (NSCLC) in patients whose tumours test positive for the EGFR-TK mutation (NICE technology appraisal guidance 192) implies that the therascreen EGFR PCR Kit is recommended and cost-effective as part of the test-treat strategy. The Committee concluded that, for the cobas EGFR Mutation Test and for Sanger sequencing-based methods, an equivalent evidence base exists, and therefore these tests and the therascreen EGFR PCR Kit can be considered clinically effective and cost-effective for informing first-line treatment decisions in patients with previously untreated, locally advanced or metastatic NSCLC in the NHS. The Committee further concluded that, for the non-Sanger sequencing-based tests (high-resolution melt analysis, pyrosequencing combined with fragment length analysis and single-strand conformation polymorphism analysis) and for tests not included in the External Assessment Group's assessment (the therascreen EGFR Pyro Kit and next-generation sequencing), the evidence was insufficient to allow any recommendations to be made on their use.

See Sections 5 and 6 in the original guideline document for additional information on cost-effectiveness.

Method of Guideline Validation

External Peer Review

Description of Method of Guideline Validation

The National Institute for Health and Care Excellence (NICE) sends the Diagnostics Assessment Report (DAR), with any confidential material removed, to registered stakeholders for comment. Stakeholders have 10 working days to return comments. Models supporting the DAR are made available to registered stakeholders on request during this period.

NICE presents anonymised registered stakeholder comments on the DAR, along with any responses from NICE or the External Assessment Group (EAG), to the Committee and later publishes these comments on its website.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

The Diagnostics Advisory Committee considered clinical and cost-effectiveness evidence from a systematic review of epidermal growth factor receptor tyrosine kinase (EGFR-TK) mutation testing in adults with locally advanced or metastatic non-small-cell lung cancer (NSCLC) prepared by an External Review Group.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate epidermal growth factor receptor tyrosine kinase (EGFR-TK) mutation testing in previously untreated adults with locally advanced or metastatic non-small-cell lung cancer (NSCLC)

Potential Harms

Epidermal growth factor receptor tyrosine kinase (EGFR-TK) tests can render false-positive and false-negative results.

Qualifying Statements

Qualifying Statements

- This guidance represents the view of the National Institute for Health and Clinical Excellence (NICE), which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.
- Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity, and foster good relations. Nothing in this guidance should be interpreted in a way which would be inconsistent with compliance with those duties.

Implementation of the Guideline

Description of Implementation Strategy

The National Institute for Health and Care Excellence (NICE) has developed tools (see also the "Availability of Companion Documents" field) to help organisations put this guidance into practice.

Implementation Tools

Mobile Device Resources

Patient Resources

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

National Institute for Health and Care Excellence (NICE). EGFR-TK mutation testing in adults with locally advanced or metastatic non-small-cell lung cancer. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Aug. 46 p. (Diagnostics guidance; no. 9).

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2013 Aug

Guideline Developer(s)

National Institute for Health and Care Excellence (NICE) - National Government Agency [Non-U.S.]

Source(s) of Funding

National Institute for Health and Care Excellence (NICE)

Guideline Committee

Diagnostics Advisory Committee

Composition of Group That Authored the Guideline

Standing Committee Members: Professor Ron Akehurst, Professor in Health Economics, School of Health and Related Research (ScHARR), University of Sheffield; Dr Trevor Cole, Consultant Clinical and Cancer Geneticist, Birmingham Women's Hospital NHS Foundation Trust; Dr Paul Collinson, Consultant Chemical Pathologist, St George's Hospital; Dr Sue Crawford, GP Principal, Chillington Health Centre; Professor Ian A Cree, Senior Clinical Advisor, Warwick Medical School, University Hospitals Coventry and Warwickshire; Professor Erika Denton, National Clinical Director for Diagnostics, NHS England, Honorary Professor of Radiology, University of East Anglia and Norfolk and Norwich University Hospital; Dr Steve Edwards, Head of Health Technology Assessment, BMJ Evidence Centre; Mr David Evans, Lay representative; Dr Simon Fleming, Consultant in Clinical Biochemistry and Metabolic Medicine, Royal Cornwall Hospital; Professor Lisa Hall, Professor of Analytical Biotechnology, University of Cambridge; Professor Noor Kalsheker, Professor of Clinical Chemistry, University of Nottingham; Dr Mark Kroese (*Vice Chair*), Consultant in Public Health Medicine, PHG Foundation, Cambridge and UK Genetic Testing Network; Dr Peter Naylor, GP, Chair Wirral Health Commissioning Consortia; Professor Adrian Newland (*Chair*); Dr Richard Nicholas, Consultant Neurologist, Honorary Senior Lecturer, Heatherwood and Wexham Park Hospitals NHS Foundation Trust; Dr Gail Norbury, Consultant Clinical Scientist, Guy's and St Thomas' NHS Foundation Trust; Ms Margaret Ogden, Lay representative; Dr Diego Ossa, Director of Market Access Europe, Novartis Molecular Diagnostics; Mr Stuart Saw, Head of Financial Strategy London, NHS England; Dr Steve Thomas, Consultant Vascular and Cardiac Radiologist at Sheffield Teaching Hospitals Foundation Trust; Mr Paul Weinberger, CEO, DiaSolve Ltd, London; Mr Christopher Wiltsher, Lay representative

Specialist Committee Members: Dr Fiona Blackhall, Consultant Medical Oncologist and Honorary Senior Lecturer, Christie Hospital NHS Foundation Trust; Mrs Mandi Elliott, Chemotherapy Nurse Specialist, Queen's Centre for Oncology and Haematology; Mr Tom Haswell, Lay Representative; Mr Paul Roberts, Consultant Cytogeneticist and Interim Head of Department, St James's Hospital; Dr Mark Slade, Consultant Respiratory Physician and Clinical Director, Papworth Hospital NHS Foundation; Dr Phillipe Taniere, Consultant Histopathologist, Queen Elizabeth Hospital Birmingham

Financial Disclosures/Conflicts of Interest

Committee members are required to submit a declaration of interests on appointment, in every year of their tenure, and at each Committee meeting, in line with the National Institute for Health and Care Excellence's (NICE's) code of practice for declaring and dealing with conflicts of interest.

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Electronic copies: Available from the National Institute for Health and Care Excellence (NICE) Web site . Also available for download as a Kindle or EPUB ebook from the NICE Web site .

Availability of Companion Documents

The following are available:

- Westwood ME, Joore MA, Whiting P, van Asselt T, Ramaekers B, Armstrong N, Misso K, Severens J, Kleijnen J. Epidermal growth factor receptor tyrosine kinase (EGFR-TK) mutation testing in adults with locally advanced or metastatic non-small-cell lung cancer: a systematic review and cost-effectiveness analysis. Diagnostics assessment report. York (UK): Kleijnen Systematic Reviews Ltd; 2012. 242 p. Electronic copies: Available from the National Institute for Health and Care Excellence (NICE) Web site .
- Westwood ME, Joore MA, Whiting P, van Asselt T, Ramaekers B, Armstrong N, Misso K, Severens J, Kleijnen J. Epidermal growth factor receptor tyrosine kinase (EGFR-TK) mutation testing in adults with locally advanced or metastatic non-small-cell lung cancer: a systematic review and cost-effectiveness analysis. Diagnostics assessment report errata. York (UK): Kleijnen Systematic Reviews Ltd; 2012. 12 p. Electronic copies: Available from the NICE Web site .
- Epidermal growth factor receptor tyrosine kinase (EGFR-TK) mutation testing in adults with locally advanced or metastatic non-small-cell lung cancer. Costing statement. London (UK): National Institute for Health and Care Excellence; 2013 Aug. (Diagnostics guidance; no. 9). 5 p. Electronic copies: Available from the NICE Web site .
- Diagnostics Assessment Programme manual. London (UK): National Institute for Health and Care Excellence; 2011 Dec. 130 p. Electronic copies: Available from the NICE Web site .

Patient Resources

The following is available:

- Epidermal growth factor receptor tyrosine kinase (EGFR-TK) mutation testing in adults with locally advanced or metastatic non-small-cell lung cancer. Information for the public. London (UK): National Institute for Health and Care Excellence (NICE); 2013 Aug. (Diagnostics guidance; no. 9). Electronic copies: Available from the National Institute for Health and Care Excellence (NICE) Web site .

NGC Status

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